



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA-2017-P-3989, FDA-2017-P-4195, FDA-2017-P-5114, FDA-2017-P-5909, FDA-2017-P-5910, and FDA-2017-P-5967]

Determination That TRINTELLIX (Vortioxetine Hydrobromide) Oral Tablet, EQ 15 Milligram Base, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that TRINTELLIX (vortioxetine hydrobromide) oral tablet, equivalent to (EQ) 15 milligram (mg) base, was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for vortioxetine hydrobromide oral tablet, 15 mg base, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Meadow W. Platt, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6228, Silver Spring, MD 20993-0002, 301-796-1830.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the “listed

drug,” which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

TRINTELLIX (vortioxetine hydrobromide) oral tablets, EQ 5 mg base, EQ 10 mg base, EQ 15 mg base, and EQ 20 mg base, are the subject of NDA 204447, held by Takeda Pharmaceuticals, USA, Inc., and initially approved on September 30, 2013. TRINTELLIX is indicated for the treatment of major depressive disorder.

TRINTELLIX (vortioxetine hydrobromide) oral tablets, EQ 5 mg base, EQ 10 mg base, and EQ 20 mg base, are listed in the “Prescription Drug Product List” section of the Orange Book, and TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base, is listed in the “Discontinued Drug Product List” section of the Orange Book. Takeda Pharmaceuticals, USA,

Inc., has never marketed TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base. In previous instances (see, e.g., 72 FR 9763 (March 5, 2007), 61 FR 25497 (May 21, 1996)), the Agency has determined that, for purposes of §§ 314.161 and 314.162, never marketing an approved drug product is equivalent to withdrawing the drug from sale.

Lachman Consultant Services, Inc.; INC Research, LLC; Locke Lord, LLP; Goodwin Procter, LLP; Cipla USA Inc.; and Apotex, Inc., submitted citizen petitions dated June 29, 2017; July 12, 2017; August 21, 2017; September 25, 2017; September 25, 2017; and September 27, 2017, respectively (Docket Nos. FDA-2017-P-3989, FDA-2017-P-4195, FDA-2017-P-5114, FDA 2017-P-5909, FDA-2017-P-5910, and FDA-2017-P-5967) (collectively, “citizen petitions”). Under 21 CFR 10.30, the citizen petitions requested that the Agency determine whether TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base, was withdrawn from sale for reasons of safety or effectiveness. Lachman Consultant Services, Inc., and INC Research also asked FDA to accept ANDAs for all four strengths of TRINTELLIX (vortioxetine hydrobromide) tablets: EQ 5 mg base, EQ 10 mg base, EQ 15 mg base, and EQ 20 mg base. Because TRINTELLIX (vortioxetine hydrobromide) oral tablets, EQ 5 mg base, EQ 10 mg base, and EQ 20 mg base, are not listed in the “Discontinued Drug Product List” section of the Orange Book, these strengths do not require a determination as to whether they were withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petitions and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base, was not withdrawn for reasons of safety or effectiveness. The petitioners have identified no data or other information suggesting that TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base, was withdrawn for

reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that this drug product was not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base, in the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to TRINTELLIX (vortioxetine hydrobromide) oral tablet, EQ 15 mg base (as well as those that refer to TRINTELLIX (vortioxetine hydrobromide) oral tablets, EQ 5 mg base, EQ 10 mg base, and EQ 20 mg base), may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: November 3, 2017.

Anna K. Abram,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.

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